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homologous recombination and wherein said splice donor sequence is spliced to a splice acceptor sequence in said activated gene in said isolated eukaryotic cell.

259. (New) The method of claim 254 wherein said vector construct is a retrovirus vector construct.

REMARKS

New claims 234-259 have been added. Support for these claims can be found in Applicants' priority specification, U.S. Application No. 08/941,223, filed September 26, 1997. Support for a transcriptional regulatory sequence operably linked to an unpaired splice donor sequence can be found in the specification, *inter alia*, in the paragraph spanning pages 6 and 7, the fourth full paragraph on page 7, the second full paragraph on page 17, and the third full paragraph on page 17. Support for the transcriptional regulatory sequence being a promoter can be found throughout the specification, but can be found, *inter alia*, in the third full paragraph on page 10, and page 24. Support for the construct not containing a poly-adenylation site operably linked to the transcriptional regulatory sequence is inherent throughout the specification in that the presence of such a sequence would prevent splicing from the splice donor to effect gene trapping and gene activation. However, this embodiment can also be found in the specification, *inter alia*, in the first full paragraph on page 18, and Figure 1, which is a schematic diagram of gene activation events described in the specification, which shows poly-adenylation achieved by means of the endogenous activated gene. Support for the construct not containing a targeting sequence is inherent and explicit throughout the specification. See, for

example, the Abstract. Support for the transcriptional regulatory sequence being operably linked to an exon is found throughout the specification, *inter alia* on page 19 and also in Figures 1-4. See also, for example, page 17. Support for the construct being a retrovirus construct can be found, *inter alia*, in the first full paragraph on page 15, in the first full paragraph on page 22, in the last paragraph on page 32, and in the third full paragraph on page 33. Support for the exon being derived from a naturally-occurring eukaryotic sequence, not encoding antibiotic resistance, and not being a reporter gene, can be found, *inter alia*, in the fourth paragraph on page 25, the paragraph spanning pages 26 and 27, and Figures 1 and 4. Support for marker genes expressed by separate promoters can be found in the specification, *inter alia*, in the figure legend for Figures 2 and 3 (page 11), in the construct of Figure 4, in the first full paragraph on page 18, the paragraph spanning pages 27 and 28, and in the first full paragraph on page 28. Accordingly, no new matter has been added with these amendments.

Accordingly, Applicants respectfully request entry of the above claims.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will

expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment is respectfully requested.

Date: 14 July 2000

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